PATENT
Docket No. 468452000300

CERTIFICATE OF MAILING BY "EXPRESS MAIL"

Express Mail Label No.: EV324254113US Date of Deposit: May 8, 2003

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. § 1.10 on the date indicated above and is addressed to: **Mail Stop AF**, Commissioner For Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Scott Stewart

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Albert Z. ABRAM

Serial No.: 09/719,662

Filing Date: January 30, 2001

For: MOUSSE COMPOSITION

Examiner: C. Ostrup

Group Art Unit: 1614

CTO
5/19/03

DECLARATION OF RONALD HARDING

PURSUANT TO 37 C.F.R § 1.132

Box AF
Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I, Ronald Harding, M.S., declare as follows:

1. I am Managing Director of E-Nova Research Pty Ltd, Australia. E-Nova is a product research and development company engaged in the management, design and development of new formulations for the pharmaceutical, personal care and household industries. My responsibilities include strategic direction, product design, project management, and formulation development. From September, 1995 to November, 2000 I was Research and Development Manager of Soltec Research Pty Ltd, Australia. Soltec is a product research and development company engaged in the design and development of new formulations for the

pharmaceutical, personal care, animal health and household industries. My responsibilities at Soltec included coordinating with manufacturing, marketing and biological functions, developing new single and mixed fungicide formulations, and scale up studies of granular formulations. Prior to that, since 1978 I worked as a formulation chemist for both SHELL FORSCHUNG GmbH, Germany and SHELL RESEARCH Ltd, United Kingdom. My responsibilities included developing a novel insecticide/polymer mix, identifying practical manufacturing processes, providing technical support to business functions, and processing trials of new formulations up to manufacturing scale in plants.

2. I received a Master of Science in Colloid and Surface Chemistry in 1992 from the University of Bristol, Avon, United Kingdom. I graduated from the Royal Society of Chemistry -Part II from Mid Kent College of Further and Higher Education, Chatham, United Kingdom in 1988. I graduated from the Royal Society of Chemistry Part I from Mid Kent College of Further and Higher Education, Chatham, United Kingdom in 1986. I received a Higher National Certificate in Chemistry from Mid Kent College of Further and Higher Education, Chatham, United Kingdom, in 1982.

3. I have reviewed the specification of United States Patent Application Serial No. 09/719,662. I am not an inventor of the subject matter claimed. I have reviewed the rejections to the pending claims set forth in the Office Action mailed from the United States Patent and Trademark Office on November 1, 2002. I have reviewed the references cited by the Examiner as the subject of rejections regarding the patentability of the claimed invention. Specifically, I have reviewed Davis, U.S. Patent No. 5,143,717 (hereafter, "the '717 patent") and Woodford *et al.*, "Bioavailability and Activity of Topical Corticosteroids from a Novel Drug Delivery System, the Aerosol Quick-Break Foam", *J. Pharm. Sci.* 66 (1) (1977).

4. The '717 patent specification does not teach using organic solvents or cosolvents in amounts sufficient to solubilize the active ingredient. In Example 1, IPM is used as an emolient in an amount of 3.28%, and on page 8, IPM is listed as an emolient in a range of 0.98% to 4.46%. To the contrary, the present specification teaches specifically adding an organic cosolvent as follows:

> The composition further includes an organic cosolvent. The organic solvent may be an ester of a fatty acid, e.g. C12 –C15 alkyl benzoate, a medium to long chain alcohol, an aromatic and/or alkyl pyrollidinone, an aromatic and/or alkyl and/or cylic ketone, an aromatic and/or alkyl and/or cyclic ether, substituted and/or unsubstituted single or multiple ring aromatic, straight chain and/or branched chain and/or cyclic alkane or silicone.
>
> The cosolvent may be present in amounts of approximately 0.25% to 50%, preferably 0.5% to 2.0%. Preferred organic cosolvents include C12-C15 alkyl benzoates (Finsolv TN) and caprylic/capric triglyceride (Crodamol GTCC). (Specification, paragraph bridging pages 5-6.)

5. Claim 1 of the presently claimed invention requires an organic cosolvent. The language "the pharmaceutically active ingredient being solubilized in the composition but insoluble in both water and the occlusive agent" necessitates the presence of an organic cosolvent in an amount sufficient to solubilize the active ingredient.

6. An organic cosolvent is not required if a pharmaceutically active ingredient is suspended in a composition instead of being dissolved. Thus the stipulation that the composition comprise an organic cosolvent is essential for the invention, and it indicates that the active ingredient is dissolved in the composition. Stated differently, if an active agent is soluble in water or an occlusive agent such as petrolatum/mineral oil, then a cosolvent would not be required and would not be included in the composition.

7. The '717 Patent teaches an aerosolised antibiotic suspended in an oil in water emulsion. The specification teaches a suspension, specifically discussing micelles. There is no discussion or teaching of solvents.

8. Solubilized active ingredients are transported across the skin faster than active ingredients in a particulate (solid) form. Particularly in the case of corticosteroids, insufficient therapeutic activity is observed if the corticosteroid is delivered to the skin as a particulate when typical therapeutic doses are used.

9. Micelles are organized aggregates of surfactant molecules as explained in Colloid and Surface Chemistry, 4th Ed., Duncan Shaw submitted herewith as Appendix 1) and can form many shapes such as spheres, tubes, layers as aggregates, vesicles and lamella. Typically in less

concentrated solutions micelles form spherical aggregates or vesicles, which will are in the form of a dispersed phase within a continuous phase.

10. Woodford *et al.* teach using 2.0 g of a ***nonionic*** emulsifying wax (not "2.0g of non-emulsifying wax" as stated on page 4 of the Final Office Action in relation to U.S. Patent Application No. 09/719,662).

11. A non-ionic emulsifying wax is a suitable foaming agent for quick break foams such as the topical dosage corticosteroid quick break aerosol foam specifically described by Woodford *et al.* Especially in the presence of dichlorodifluoromethane and dichlorotetrafluoroethane, an aqueous alcohol system incorporating a non-ionic emulsifying wax may be used to prepare a quick break foam provided the alcohol-water ratio is between approximately 50:50 and 70:30.

12. The term "wax" is not synonymous with occlusion. Wax describes general physical properties and physical states (*See, e.g.*, Lenick, *et al.*, "Primary Ingredients" submitted herewith as Appendix 2). The generally accepted classification for oils, waxes and butters requires that the material be insoluble in water and have an appropriate physical state. An example of such a material is silicone wax 580 from Dow Corning. This material is insoluble in water, but is not occlusive as explained in the Dow Corning literature (submitted herewith as Appendix 3).

13. The formulations of Woodford *et al.* were occluded with a polyester film. Some sites were left nonoccluded, but these were protected by plastic to avoid the hydrating effect of occlusion.

14. Woodford *et al.* do not teach including an occlusive agent as claimed in the present application. Woodford *et al.* state that the actual nonionic emulsifying wax used was Polarwax A31 manufactured by Croda Chemicals. Information from Croda and the Cosmetic and Toiletries Bench Reference reveal that this wax is a mixture of cetostearyl alcohol and a polyoxyethylene derivative of a sorbitan fatty acid ester (*See* Appendix 4, submitted herewith). Neither a cetostearyl alcohol nor a polyoxyethylene derivative of a sorbitan fatty acid ester are considered occlusive agents. A polyoxyethylene derivative of a sorbitan fatty acid ester is a

medium to high HLB surfactant with good water affinity. Cetostearyl alcohol, although a long chain alkane, has a hydroxyl group attached at the end of the chain. This imparts significant polarity and hydrophilicity to the molecule. Hence, this property would allow easy transmission of water across a film made from this material. Although the wax (Polarwax) of Woodford *et al.* is precipitated onto the skin is not occlusive.

15. A polyester or food wrap film is often used when assessing the efficacy and bioavailability of an active ingredient in a composition. This type of cover provides occlusion, and the performance of active ingredients is normally enhanced when tested under occlusion. Woodford *et al.* use a polyester film for occlusion and not just as a protective barrier. In fact, Woodford *et al.* use a plastic guard to offer protection against external influences but not occlusion in a subsequent set of tests in the cited article.

16. A number of commercially available products use occlusion to achieve acceptable performance. Two such products, Emla Cream and Nicotine patches, use occlusive techniques to achieve efficacy. The consumer information sheet for Emla cream (submitted herewith as Appendix 5) stipulates the use of such a plastic food wrap or the like over the composition after application for this very purpose.

17. The mechanism of a quick break foam is well known. Woodford *et al.* describe the accepted mechanism as follows:

> "When the foam product is discharged from the container, the propellant is vaporized; the foaming agent (nonionic emulsifying wax) crystallized due to a loss of solubilizer (*i.e.*, propellant) and a reduction in temperature to below that at which the foaming agent deposited. The precipitation of the wax from solution produced a foam that collapsed on the skin as the wax redissolved at skin temperature".

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to by true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

05 May 2003
Date

Ronald Harding, M.S.